Peer review file

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Reviewer A

Comment 1: How do the authors manage the cough during the procedure?

Reply 1: Thank you for this question. The cough during the procedure was suppressed by low dose remifentanil and a very small intravenous boluses of propofol (10mg) according to Kim et al., Anaesthesia 2010 Jul;65(7):697-703.

Changes in the text: Page 5 and reference 10.

Comment 2: After stent deployment, do the authors notice cardiac alteration? If yes, how do they manage it? I had two cardiac arrests after insertion of Y stent.

Reply 2: No did not observe any cardiac abnormalities.

Comment 3: Under spontaneous breathing, a collapse of posterior tracheal wall may occur making challenging the identification of distal airway and the insertion of the stent. Do the authors use fluoroscopy to insert the stent?

Reply 3: Yes, we used fluoroscopy in each of the three cases.

Changes in the text: We added “fluoroscopy” in each case presentation.

Comment 4: I know that tracheo-esophageal fistula is a dramatic clinical condition with a very poor prognosis. However, the results reported by the authors are poor considering that one patient died 2 weeks after the procedure and another one week after the procedure. If the main cause was the disease progression (as reported by the authors), in theory the insertion of Y stent failed to treat the tracheo-esophageal fistula.

Reply 4: This is, indeed, a difficult question. Retrospectively, one could conclude that stent placement could prolong survival in 2/3 cases. However, there was no choice,

except best supportive care. And, the patients themselves felt relief of their severe symptoms. As such, stent placement was a successful palliative treatment.

Reviewer B

Comment 1: Conscious sedation should be changed to moderate sedation as per American Society of Anesthesiologists guidelines.

Reply 1: Thank you for this very valuable comment. We changed this in the text accordingly.

Changes in the text: Several.

Comment 2: The authors state that stent insertion requires apnea which is untrue. There will be apnea if the airway is blocked by the stent but this is true for both general anesthesia and moderate sedation with spontaneous breathing. Ventilation can typically be maintained during stent insertion.

Reply 2: It is true that stent placement is feasible during maintained ventilation. However, we described the "traditional" technique in apnea to compare with our new approach to highlight the risks of maintained ventilation.

Comment 3: The authors should describe the FiO2 used for the patients during the bronchoscopy.

Reply 3: A very interesting question, thank you. An estimation of the FiO2 via face mask and O2 application via the bronchoscope is difficult. Before the intervention, the patients were pre-oxygenated with a face mask. Oxygen delivery during the procedure was maintained with face mask and through the bronchoscope. We added this to the text.

Changes in the text: Page 5.

Reviewer C

Comment 1: I carefully reviewed your manuscript which I think offers novel insights into performing rigid bronchoscopy. I would simply suggest the title be changed to "dexmedetomidine-assisted sedation with spontaneous ventilation" as other anesthesia drugs were used in all cases.

Reply 1: Basically, we agree with this comment. However, we decided to leave the title unchanged, since it reads much better like this. In addition, the original title does not preclude the use of other drugs.

Reviewer D

Comment 1: Whenever a novel technique is presented, it is important to provide a thorough description of the procedure to allow the reader to properly assess the technique as well as replicate the technique for additional investigation. I would ask the authors to provide much more detail about how sedation is achieved to allow rigid bronchoscopy to be performed safely and with minimal discomfort to the patient.
- Was topical lidocaine used to anesthetize the oropharynx? If so, how was this administered and how much was given? If not, how was coughing and gagging minimized during the procedure to minimize risk of patient discomfort and regurgitation?

Reply 1: Thank you very much for this important question. Due to restrictions on word count, there was very limited space to go into details here. However, we added the use of lidocaine, since we believe this was a relevant contributor successful treatments.

Changes in the text: Page 5.

Comment 2: How was the rigid bronchoscope safely advanced past the vocal cords and thru the glottis? In an awake patient, there can be laryngospasm and coughing that can cause severe vocal cord injury during intubation with rigid bronchoscope.

Reply 2: This is indeed a crural point, thank you for asking. We administered slight boli of propofol (10 – 20mg) during the insertion of the rigid bronchoscope. In addition, we used local anesthesia using lidocaine. This has been added to the text.

Changes in the text: Page 5.

Comment 3: How was coughing minimized during the procedure to allow for safe stent deployment?

Reply 3: Thank you for this question. The cough during the procedure was suppressed by low dose remifentanil and a very small intravenous boluses of propofol (10mg).

Changes in the text: Page 5.

Comment 4: How was the patient monitored during the procedure for adequate ventilation and sedation? Was end tidal CO2 measured? If so, how was this measured?

Reply 4: The patient has been monitored with ECG, arterial line to measure blood pressure and arterial O2 and CO2, and oxygen saturation. Because of the open system the endtidal CO2 has only be measured at the beginning and the end of the procedure.

Changes in the text: Page 5.

Comment 5: How was supplemental oxygen administered to the patient? Was an open or closed ventilator system used for the procedure?

Reply 5: Pre-oxygenation was done with a face mask. Oxygen delivery during the procedure was maintained with face mask and through the bronchoscope. Both are open systems.

Changes in the text: Page 5.

Comment 6: The intraoperative risks of this technique are two fold: (1) undersedation

leading to significant patient discomfort and cough and (2) oversedation leading to hypoventilation. How would the authors recommend we address these complications if they are to occur? What are the backup plans for patient sedation and ventilation/oxygenation if we are to encounter these situations? When would the authors recommend we abort the plan for conscious sedation and utilize an alternative anesthetic strategy?

Reply 6: Thank you for this question, which addresses an important issue during the procedure. We monitored the sedation with clinical parameters (RASS, respiratory rate, movements, heart rate and blood pressure) in terms of a good clinical judgement. This requires an experienced anesthesiologist. We have got frequent sedations in NIVATS (non-intubated videoassisted thoracic surgery) cases with similar requirements. Both under- and oversedation would have ended up in a back-up plan consisting of deep sedation and jet ventilation through the rigid bronchoscope.

Changes in the text: Page 5

Comment 7: The authors state that all patients tolerated the procedure well without any evidence of pain, discomfort, dyspnea, etc. How was this determined? What objective or subjective measures were utilized to confirm this? Were validated assessment tools used to determine patient comfort?

Reply 7: Thank you for asking, the intraoperative tolerance has been measured with the RASS, postoperative we assessed the NAS, the absence of PONV and the time to discharge from the PACU (post anesthesia care unit).

Comment 8: Proper patient selection is likely critical for success in a novel technique such as this. What considerations (aside from avoiding jet ventilation) would the authors suggest we use to determine appropriate patient candidacy?

Reply 8: The most relevant prerequisites for this technique is ensuring that anatomy allows intubation with a rigid bronchoscopy (oral opening, reclination) and a trustful patient-doctor relation. Furthermore, the patient must be informed that he will not be

able to speak during the procedure. Thus, a clear hand signaling must be arranged. We added this important information to the text.

Changes in the text: Page 5

Comment 9: How was informed consent performed in this setting? Were patients notified that they were undergoing a novel approach to rigid bronchoscopy and were they properly explained the risks, benefits, and alternatives to this technique?

Reply 9: The novel method has been stated in the written informed consent with the patient, the pneumologist and the anesthesiologist. All patients gave a general consent for research.

Changes in the text: Page 2

Reviewer E

Comment 1: I read with great interest the case series by Kowalski et al that reported the use of dexmedetomidine in patients undergoing rigid bronchoscopy for malignant airway fistula. The authors describe 3 cases where dexmedetomidine was used in conjunction with other agents to facilitate rigid bronchoscopy and stent placement. The patient's tolerated the procedure well and had procedure related success without any known adverse events.

While the cases are interesting, the multiple terminologies are used in the paper, which create confusion in terms of what the authors are trying to convey. The authors in the introduction of the letter state that general anesthesia and jet ventilation required for RB may cause, gastric distension and pneumomediastinum or worsening of fistula. While the use jet ventilation can lead to the problem, it is unclear how the use of a general anesthetic without endotracheal intubation ventilation would lead to this issue, especially if the patient is breathing spontaneously. The author's reference # 4 (Shamji et al) did not explain the details either. The authors then mention in line # 30 that they used conscious sedation and spontaneous respiration using dexmedetomidine to seal the TEF/TMF.

Subsequently, in the cases the authors mention that patients were titrated to a RASS score of -1 to -2 during induction. They then mention in case 1 that a continuous infusion with Remifentanil and dexmedetomidine was used. In addition, a "few" propofol boli were used. The authors mention Table 1 which is not included with the manuscript. In case 2, Anesthesia was provided using the identical drug and dose regimen as in case 1. In case 3, several propofol boli, remifentanil and continuous infusion of dexmedetomidine were used. While the authors claim that conscious sedation was provided using dexmedetomidine, the drug combination of Remifentanil, profofol and dexmedetomidine was used in all cases rather than dexmedetomidine alone. This would qualify as total intravenous anesthesia (TIVA) rather than conscious sedation. In rigid bronchoscopy, when the rigid bronchoscope can be used for ventilation, and thus endotracheal intubation is not required, there is no difference between this and the use of TIVA with spontaneous ventilation as was described in the recent study by Murgu et al.

In the discussion section the authors initially claim that "Our three patients with severe TEF or TMF tolerated RB using dexmedetomidine without pain or stress". In the subsequent line the authors state that, "During potentially painful or stressful periods, the effect of dexmedetomidine was supplemented with Remifentanil and propofol". This is a confusing message and does not clarify what exactly the authors are trying to convey by the means of this report.

Finally, the authors conclude that, "In conclusion, the use of dexmedetomidine was of great benefit for the patients and confirmed the results of previous studies regarding spontaneous respiration and conscious sedation". I don't believe either of those conclusions can be made based on this case series. While interesting, I don't believe the message that the authors are trying to convey is thoroughly conveyed by the description used in the series. This manuscript will benefit from changes that would better clarify the intended message.

Reply 1: Many thanks for these important remarks. First of all, we apologize that Table 1 had been lost. We now added Table 1 within the revised manuscript.

Concerning the wording, we have changed to term conscious sedation into moderate sedation throughout the manuscript. In fact, we describe a moderate sedation using a combination of three intravenous anesthetics, whereas dexmedetomidine is the cornerstone. Therefore, the term TIVA would also be justified. However, we decided to avoid this term to emphasize that the patients were arousable during the procedure.

We regret that Reviewer E questions the success of our technique. However, we insist on the wording of our findings, since both operator and patients felt it was beneficial. In addition, we cannot find a confusing message in the discussion, since we stated that in potentially painful or stressful periods, the effect of dexmetedomidine was supplemented by other drugs. Eventually, this anticipatory approach prevented the patients from discomfort.